

CLAIMS

What is claimed is:

5 1. A method of making a cationic nonviral delivery vehicle, said method comprising,

 mixing together a steroid or a modification or derivative thereof, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said steroid or a modification or derivative thereof with said polyamine,

10 purifying said conjugated steroid-polyamine molecule, and

 mixing said steroid-polyamine molecule with a lipid, thereby producing a cationic nonviral delivery vehicle.

15 2. The method of claim 1, wherein dimethylsulfoxide is mixed with said steroid or a modification or derivative thereof, said conjugating reagent, and said polyamine.

20 3. The method of claim 1, wherein said steroid is selected from the group consisting of a glucocorticoid, a mineralcorticoid, an androgen, an estrogen, a progestagen, an analog with steroidal agonist activity, an analog with steroidal antagonist activity, an inactive structural analog, and modifications or derivatives thereof.

25 4. The method of claim 1, wherein said steroid is selected from the group consisting of a cationic steroid and a cationic steroid prodrug.

30 5. The method of claim 1, wherein said cationic nonviral delivery vehicle binds with an anionic domain of a molecule selected from the group consisting of a glycosaminoglycan, a collagen, a fibrin, a cellular glycocalyx, a red blood cell glycocalyx, a sialic acid, a sulfated glycocalyx, and an isolated nucleic acid.

6. The method of claim 5, wherein said glycosaminoglycan is hyaluronic acid.

7. The method of claim 1, wherein said steroid is selected from the group
5 consisting of dexamethasone, 11-deoxycorticosterone-21-mesylate, corticosterone-21-
mesylate, 11-deoxycortisol-21-mesylate, cortisol-21-mesylate, tamoxifen, 4-hydroxy
tamoxifen, 21-chloro-17hydroxyprogesterone, cholesterol tosylate, hydrocortisone
mesylate, 17 α -mesylate-estradiol-3-acetate, and dexamethosone-21-mesylate.

10 8. The method of claim 7, wherein said steroid is dexamethasone.

9. The method of claim 7, wherein said steroid is dexamethasone-21-
mesylate.

15 10. The method of claim 1, wherein said steroid is a mesylate derivative.

11. The method of claim 1, wherein said conjugating reagent is 2-
iminothiolane.

20 12. The method of claim 1, wherein said polyamine is selected from the
group consisting of spermine, a polylysine, lysine, a lysine containing peptide, an
arginine containing peptide, a cationic polymer, and an amine rich polymer.

25 13. The method of claim 12, wherein said cationic polymer is
polyethyleneimine (PEI).

14. The method of claim 1, wherein said lipid is a neutral lipid.

15. The method of claim 1, wherein said lipid is a helper lipid.

30

16. The method of claim 15, wherein said neutral lipid is selected from the group consisting of dioleylphosphatidylethanolamine (DOPE), phospahtidyl choline (PC) and cholesterol.

5 17. The method of claim 1, wherein said lipid is a cationic lipid.

18. The method of claim 17, wherein said cationic lipid is selected from the group consisting of 3-beta-[N',N'dimethylaminoethane)-carbamoyl]cholesterol) (DC-Chol), N[1-(2,3-dioleyloxy)propyl [N,N,N-triethyl-ammonium (DOTMA), 2'-(1'',2''-dioleyloxypropyldimethyl-ammonium bromide)-N-ethyl-6-amindospermine tetra trifluoroacetic acid (DOSPA) , 1,3-bis(oleoyloxy)-3-(trimethylammonio)propane (DOTAP), and GL-67.

10 19. A cationic nonviral delivery vehicle comprising a dexamethasone-spermine molecule and a lipid.

15 20. A cationic lipid nonviral delivery vehicle made by the method of claim 1.

20 21. A composition comprising a cationic nonviral delivery vehicle produced by the method of claim 1 and a pharmaceutically acceptable carrier.

25 22. A method of making a cationic nonviral delivery vehicle, said method comprising,

mixing together a drug or a modification or derivative thereof, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said drug or a modification or derivative thereof with said polyamine, purifying said conjugated drug-polyamine molecule, and mixing said drug-polyamine molecule with a lipid, thereby producing a cationic nonviral delivery vehicle.

23. The method of claim 22, wherein dimethylsulfoxide is mixed with said drug or a modification or derivative thereof, said conjugating reagent, and said polyamine.

5

24. The method of claim 22, wherein said drug is a hydrophobic drug.

25. The method of claim 22, wherein said drug is a mesylate derivative.

10 26. The method of claim 22, wherein said drug is selected from the group consisting of a cationic drug and a cationic prodrug.

27. A cationic lipid nonviral delivery vehicle made by the method of claim 22.

15

28. A kit for administering a cationic nonviral delivery vehicle, wherein said cationic nonviral delivery vehicle is made by mixing together a steroid or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said steroid or a modification or derivative thereof with said polyamine, purifying said conjugated steroid-polyamine molecule, and mixing said steroid-polyamine molecule with a lipid, said kit comprising a cationic nonviral delivery vehicle, an applicator, and an instructional material for the use thereof.

20

29. A kit for administering a cationic nonviral delivery vehicle, wherein said cationic nonviral delivery vehicle is made by mixing together a drug or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said drug or a modification or derivative thereof with said polyamine, purifying said conjugated drug-polyamine molecule, and mixing said drug-polyamine molecule with a lipid,

30

5 said kit comprising a cationic nonviral delivery vehicle, an applicator, and an instructional material for the use thereof.

10 30. A method for facilitating delivery of a compound to a cell, said method comprising administering to said cell a composition comprising said compound and an effective amount of a cationic nonviral delivery vehicle,

15 wherein said cationic nonviral delivery vehicle is made by mixing together a steroid or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said steroid or a modification or derivative thereof with said polyamine, purifying said conjugated steroid-polyamine molecule, and mixing said steroid-polyamine molecule with a lipid,

20 further wherein said delivery vehicle facilitates delivery of said compound to said cell, thereby facilitating delivery of said compound to said cell.

25 31. A method for facilitating delivery of a compound to a cell, said method comprising administering to said cell a composition comprising said compound and an effective amount of a cationic nonviral delivery vehicle,

30 wherein said cationic nonviral delivery vehicle is made by mixing together a drug or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said drug or a modification or derivative thereof with said polyamine, purifying said conjugated drug-polyamine molecule, and mixing said drug-polyamine molecule with a lipid,

35 further wherein said delivery vehicle facilitates delivery of said compound to said cell, thereby facilitating delivery of said compound to said cell.

40 32. A method for facilitating delivery of a compound to a tissue, said method comprising administering to said tissue a composition comprising said compound and an effective amount of a cationic nonviral delivery vehicle,

45 wherein said cationic nonviral delivery vehicle is made by mixing together a steroid or a modification or derivative thereof, dimethylsulfoxide, a conjugating

reagent, and a polyamine, wherein said conjugating reagent conjugates said steroid or a modification or derivative thereof with said polyamine, purifying said conjugated steroid-polyamine molecule, and mixing said steroid-polyamine molecule with a lipid,

5 further wherein said delivery vehicle facilitates delivery of said compound to said tissue, thereby facilitating delivery of said compound to said tissue.

33. The method of claim 32, wherein said compound binds an anionic constituent of said tissue, further wherein said compound is slowly released from the delivery vehicle.

10

34. The method of claim 32, wherein said delivery vehicle binds an anionic constituent of said tissue, further wherein said compound is slowly released from the delivery vehicle.

15

35. A method for facilitating delivery of a compound to a tissue, said method comprising administering to said tissue a composition comprising said compound and an effective amount of a cationic nonviral delivery vehicle,

wherein said cationic nonviral delivery vehicle is made by mixing together a drug or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, 20 and a polyamine, wherein said conjugating reagent conjugates said drug or a modification or derivative thereof with said polyamine, purifying said conjugated drug-polyamine molecule, and mixing said drug-polyamine molecule with a lipid,

further wherein said delivery vehicle facilitates delivery of said compound to said tissue, thereby facilitating delivery of said compound to said tissue.

25

36. The method of claim 35, wherein said compound binds an anionic constituent of said tissue, further wherein said compound is slowly released from the delivery vehicle.

37. The method of claim 35, wherein said delivery vehicle binds an anionic constituent of said tissue, further wherein said compound is slowly released from the delivery vehicle.

5 38. The method of claim 32, wherein said tissue is selected from the group consisting of muscle, mucosa, epithelial, nerve, connective, blood, stromal, heart, liver, kidney, skin, brain, intestinal, interstitial space, bone, bone marrow, joint, cartilage, tendon, esophagus, gonad, cerebrospinal fluid, pancreas, spleen, ocular, nasal cavity, and hair.

10 39. The method of claim 30, wherein said cell is a mammalian cell.

40. The method of claim 39, wherein said mammalian cell is a human cell.

15 41. The method of claim 40, wherein said cell is selected from the group consisting of an endothelial cell, a mesenchymal cell, a neural cell, a fibroblast, neuron, a smooth muscle cell, a kidney cell, a liver cell, a myoblast, a stem cell, an embryonic stem cell, a hematopoietic stem cell, an osteoblast, a chondrocyte, a chondroblast, a monocyte, 20 a neutrophil, a macrophage, a retinal nerve cell, and an epithelial cell.

42. The method of claim 30, wherein said compound is selected from the group consisting of a nucleic acid, a recombinant protein, erythropoietin, tissue plasminogen activator (tPA), tumor necrosis factor-alpha receptor, Omeprazole, Simvastatin, Atorvastatin calcium, Amlodipine besylate, Loratadine, Lansoprazole, 25 Epoetin alfa, Celecoxib, Fluoxetine hydrochloride, Olanzapine, Paroxetine hydrochloride, Rofecoxib, Sertraline hydrochloride, Epoetin alfa, a conjugated estrogens, Amoxicillin and clavulanate Potassium, Pravastatin sodium, Enalapril maleate, Metformin hydrochloride, Pravastatin, Losartan potassium, Ciprofloxacin hydrochloride, Risperidone, Paclitaxel, Azithromycin, interferon alpha-2b, rebavirin, Sildenafil citrate,

Gabapentin, Fluticasone propionate, Alendronate sodium, Clarithromycin, Filgrastim, cyclosporine, Lisinopril dihydrate, venlafaxine HCl, human insulin, Levofloxacin, Fexofenadine, Hydrochloride, Lisinopril/lisinopril, Sumatriptan succinate, Nifedipine, Fluconazole, Ceftriaxone sodium, Famotidine, Enoxaparin sodium, Leuprolide acetate, 5 Salmeterol xinafoate, Clopidogrel bisulfate, Lansoprazole, and Ranitidine.

43. The method of claim 42, wherein said nucleic acid is selected from the group consisting of a plasmid, an expression vector, an oligonucleotide, an antisense oligonucleotide, a PCR product, a DNA-RNA chimera, a peptide-nucleic acid (PNA), 10 RNA interference (RNAi), and an isolated nucleic acid.

44. The method of claim 43, wherein said isolated nucleic acid is DNA.

45. The method of claim 30, wherein said cell is not in a mammal.

15 46. The method of claim 30, wherein said cell is in vivo in a mammal.

47. The method of claim 30, wherein said composition is administered via a route selected from the group consisting of topical, oral, subcutaneous, intranasal, 20 rectal, vaginal, intramuscular, and intravenous.

48. A method of treating a disease or disorder in a mammal, said method comprising administering to said mammal a composition comprising a cationic nonviral delivery vehicle and an effective amount of a compound,

25 wherein said cationic nonviral delivery vehicle is made by mixing together a steroid or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said steroid or a modification or derivative thereof with said polyamine, purifying said conjugated steroid-polyamine molecule, and mixing said steroid-polyamine molecule with a lipid,

further wherein said compound treats said disease or disorder, thereby
treating a disease or disorder in a mammal.

49. The method of claim 48, wherein an effective amount of said
5 compound or an effective amount of another compound is also delivered by a vehicle
other than said cationic delivery vehicle.

50. The method of claim 48, wherein said disease or disorder is selected
from the group consisting of inflammation, asthma, arthritis, pain, inflammation of a
10 joint, cancer, allergy, hypertension, hyperplasia, metastasis, claudication, intimal
hyperplasia, hemophilia, a coagulopathy, an autoimmune disorder, an ulcer, erosive
esophagitis, a heart disease or condition, a pathological hypersecretory condition, rhinitis,
chronic idiopathic urticaria, a hypersecretory condition, heartburn, an infection, familial
adenomatous polyposis, depression, obsessive-compulsive disorder, bulimia nervosa,
15 premenstrual dysphoric disorder, a psychotic disorder, schizophrenia, psychotic
disorders, bipolar disorder, obsessive-compulsive disorder, generalized anxiety disorder,
panic disorder, social anxiety disorder, dysmenorrhea, pain, posttraumatic stress disorder,
panic disorder, anemia, menopausal symptoms, osteoporosis, hypoestrogenism, Kraurosis
vulvae, hypercholesterolemia, type II diabetes, Kaposi sarcoma, warts, hepatitis C,
20 hepatitis B, erectile dysfunction, epilepsy, Paget disease, neutropenia, progenitor cell
mobilization, organ transplant rejection, psoriasis, cluster headache, migraine, angina,
hypertension, candidiasis, gastritis, a cardiac ischemic complication, endometriosis,
central precocious puberty, bronchospasm, gastro-esophageal reflux disease,
mastocytosis, and a proliferative disorder.

25
51. A method of treating a disease or disorder in a mammal, said method
comprising administering to said mammal a composition comprising a cationic nonviral
delivery vehicle and an effective amount of a compound,
wherein said cationic nonviral delivery vehicle is made by mixing together
30 a drug or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent,

and a polyamine, wherein said conjugating reagent conjugates said drug or a modification or derivative thereof with said polyamine, purifying said conjugated drug-polyamine molecule, and mixing said drug-polyamine molecule with a lipid,

further wherein said compound treats said disease or disorder, thereby
5 treating a disease or disorder in a mammal.

52. A kit for treating a disease or disorder in a mammal, said kit comprising a cationic lipid nonviral delivery vehicle, and an effective amount of a compound, an applicator, and an instructional material for the use thereof,

10 wherein said compound treats said disease or disorder,

further wherein said cationic nonviral delivery vehicle is made by mixing together a steroid or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said steroid or a modification or derivative thereof with said polyamine, purifying the steroid-polyamine molecule, and mixing said steroid-polyamine molecule with a lipid.

53. A kit for treating a disease or disorder in a mammal, said kit comprising a cationic lipid nonviral delivery vehicle, and an effective amount of a compound, an applicator, and an instructional material for the use thereof,

20 wherein said compound treats said disease or disorder,

further wherein said cationic nonviral delivery vehicle is made by mixing together a drug or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said drug or a modification or derivative thereof with said polyamine, purifying the drug-polyamine molecule, and mixing said drug-polyamine molecule with a lipid.

25 54. A method for facilitating incorporation of a compound into a cell, said method comprising administering to said cell said compound and an effective amount of a cationic lipid nonviral delivery vehicle, wherein said cationic nonviral delivery vehicle is made by mixing together a steroid or a modification or derivative thereof,

dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said steroid or a modification or derivative thereof with said polyamine, purifying the steroid-polyamine molecule, and mixing said steroid-polyamine molecule with a lipid, further wherein said delivery vehicle facilitates incorporation of said compound into said cell, thereby facilitating incorporation of said compound into said cell.

5 55. A method for facilitating incorporation of a compound into a cell, said method comprising administering to said cell said compound and an effective amount of a cationic lipid nonviral delivery vehicle, wherein said cationic nonviral delivery vehicle is made by mixing together a drug or a modification or derivative thereof, dimethylsulfoxide, a conjugating reagent, and a polyamine, wherein said conjugating reagent conjugates said drug or a modification or derivative thereof with said polyamine, purifying said conjugated drug-polyamine molecule, and mixing said drug-polyamine molecule with a lipid, further wherein said delivery vehicle facilitates incorporation of said compound into said cell, thereby facilitating incorporation of said compound into said cell.